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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/676,045

09/30/2003

Yaron Ilan

Enz-63(CIP)

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EXAMINER

SKELDING, ZACHARY S

ART UNIT

PAPER NUMBER

1644

MAIL DATE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/676,045	<b>Applicant(s)</b> ILAN ET AL.	
	<b>Examiner</b> ZACHARY SKELDING	<b>Art Unit</b> 1644	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 27 October 2010.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 2,3,6,7,9-11,13,30-32 and 168-184 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                    | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

Continuation of Disposition of Claims: Claims pending in the application are 1-3,5-7,9-11,13,16-18,20,23,25-46,50-63,66-72,83-126,143,152-164 and 167-186.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 1,5,16-18,20,23,25-29,33-46,50-63,66-72,83-126,143,152-164,167,185 and 186.

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### DETAILED ACTION

1. Applicant's amendment and remarks filed October 27, 2010 are acknowledged.

Claims 4, 8, 12, 14, 15, 19, 21, 22, 24, 64, 65, 73-82, 127-142, 144-151, 165 and 166 have been canceled.

Claims 2, 3, 6, 7, 9-11, and 30-32 have been amended.

Claims 167-186 are newly added.

Claims 1-3, 5-7, 9-11, 13, 16-18, 20, 23, 25-46, 50-63, 66-72, 83-126, 143, 152-164 and 167-186 are pending.

Claims 1, 5, 16-18, 20, 23, 25-29, 33-46, 50-63, 66-72, 83-126, 143 and 152-164 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on March 10, 2008.

Moreover, new claim 167 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Group (Group III), there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on March 10, 2008.

Furthermore, new claims 185 and 186 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species of disease, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on March 10, 2008.

Claims 2, 3, 6, 7, 9-11, 13, 30-32, and 168-184 are under consideration wherein the species of "immune-related or immune-mediated disorders or diseases" is "autoimmune liver disease" or "Crohn's disease".

2. The claims as amended appear to no longer encompass in their breadth the prior elected species of "culture conditions for the ex vivo education of NKT".

The following amended claims illustrate the issue at hand:

Claim 2. A method for the treatment of immune-related or immune-mediated disorders or diseases in a mammalian subject in need of such treatment, by the method comprising manipulating the NKT cell population of said subject, wherein manipulation of said NKT cell population results in modulation of the Th1/Th2 cell balance towards an anti-inflammatory response, said modulation being mediated by proteins extracted from tissue affected by the

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immune- related disorder, or at least one liver-associated cell of tolerized or non-tolerized subjects suffering from said immune-related or immune-mediated disorder or of said subject.

Claim 6. The method of claim 2 or 3 comprising the steps of:

- a. obtaining NKT cells from said subject or another subject;
- b. ex vivo educating the NKT cells obtained in step (a) such that the resulting educated NKT cells may modulate the Th1/Th2 cell balance toward anti-inflammatory cytokine producing cells; and
- c. re-introducing to said subject the educated NKT cells obtained in step (b).

Claim 7. The method of claim 6, wherein said ex vivo education of step (b) is performed by culturing said NKT cells in the presence of the proteins or the liver-associated cells.

Claim 168. The method of claim 2 or 3, wherein the NKT cell population is manipulated by ex vivo culturing of NKT cells from the NKT cell population in the presence of the proteins or the liver-associated cells such that the resulting educated NKT cells may modulate the Th1/Th2 cell balance toward anti-inflammatory cytokine producing cells, then re-introducing to said subject the educated NKT cells.

Claim 169. The method of claim 7 or 168, wherein the NKT cells are cultured in the presence of the liver-associated cells.

Claim 170. The method of claim 7 or 168, wherein the NKT cells are cultured in the presence of both the proteins and the liver-associated cells.

The language of claim 7, “wherein said ex vivo education of step (b) is performed by culturing said NKT cells in the presence of the proteins or the liver-associated cells,” which is dependent from parent claim 2 which recites “said modulation being mediated by proteins extracted from tissue affected by the immune-related disorder, or at least one liver-associated cell of tolerized or non-tolerized subjects suffering from said immune-related or immune-mediated disorder or of said subject,” clearly limits the claimed methods to using “proteins extracted from tissue...” **OR** “at least one liver-associated cell...” to educate / modulate the NKT cells.

Claims 168 and 169 are also consistent with this interpretation.

However, claim 170 recites “The method of claim 7 or 168, wherein the NKT cells are cultured in the presence of both the proteins and the liver-associated cells” which seems to contradict the language of the parent claims.

That said, since the vast majority of the claims seem to limit the claimed methods to using “proteins extracted from tissue...” **OR** “at least one liver-associated cell...” to educate / modulate the NKT cells it will be assumed that this is what applicant intends to claim.

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Thus, by the claim amendments filed October 27, 2010 applicant has deleted the prior elected species of “culture conditions for the ex vivo education of NKT” which used “allogeneic antigens obtained from donors suffering from said immune-related or immune-mediated disease”, “Kupffer cells” and “IL4” from the breadth of the claimed method. Rather, the claims as amended now encompass the species of method employing “culture conditions for the ex vivo education of NKT” which use **either** “proteins extracted from tissue affected by the immune- related disorder” **OR** “at least one liver-associated cell of tolerized or non-tolerized subjects suffering from said immune-related or immune-mediated disorder or of said subject.”

Given this fact pattern and the guidance presented in the final paragraph of MPEP § 821.03 it would not be appropriate to restrict applicant only to the previously elected species of invention (which is now canceled from the currently pending claims).

That said, applicant’s amendment to the claims has necessitated the new election of species requirements put forth below.

### **Election/Restrictions**

3. This application contains claims directed to the following patentably distinct species:
4. Methods for the treatment of immune-related or immune-mediated disorders or diseases in a mammalian subject in need of such treatment, said method comprising manipulating the NKT cell population of said subject by a. obtaining NKT cells from said subject or another subject;  
b. ex vivo educating the NKT cells obtained in step (a) such that the resulting educated NKT cells may modulate the Th1/Th2 cell balance toward anti-inflammatory cytokine producing cells; and  
c. re-introducing to said subject the educated NKT cells obtained in step (b), wherein said ex vivo education of step (b) is performed by culturing said NKT cells in the presence of

species 1, “proteins extracted from tissue affected by the immune- related disorder” or

species 2, “at least one liver-associated cell of tolerized or non-tolerized subjects suffering from said immune-related or immune-mediated disorder or of said subject”.

Method using these different species of culture conditions for the ex vivo education of NKT are independent or distinct because the structures, physicochemical properties and/or mode of action of species 1 and 2 are different, and they do not share a common structure that is disclosed to be essential for common utility. In addition, these species are not obvious variants of each other based on the current record.

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Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, or a single grouping of patentably indistinct species, for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

5. Should applicant elect the species 1 or 2 above, applicant must further elect a sub-species of "proteins" OR "liver-associated cells" selected from among the various sub-species recited in claim 9, allogeneic antigens" OR "xenogenic antigens" etc. (proteins) or claims 175 and 176, "Kupffer cell" OR "stellate cell" etc. (liver-associated cells).

Method using these different species of culture conditions for the ex vivo education of NKT are independent or distinct because the structures, physicochemical properties and/or mode of action of these species are different, and they do not share a common structure that is disclosed to be essential for common utility. In addition, these species are not obvious variants of each other based on the current record.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, or a single grouping of patentably indistinct species, for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

6. Should applicant elect the species of 1 or 2 above, applicant must FURTHER elect if the NKT cells cultured with species 1 or species 2 are further culture in the presence of "at least one cytokine" OR "the adhesion molecule selection" OR "at least one cytokine and the adhesion molecule selection" OR "NOT cultured in the presence of at least one cytokine OR the adhesion molecule selection."

Method using these different species of culture conditions for the ex vivo education of NKT are independent or distinct because the structures, physicochemical properties and/or mode of action of these species are different, and they do not share a common structure that is disclosed to be essential for common utility. In addition, these species are not obvious variants of each other based on the current record.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, or a single grouping of patentably indistinct species, for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

7. Should applicant elect the NKT cells cultured with species 1 or species 2 are further cultured in the presence of "at least one cytokine" OR "at least one cytokine and the adhesion molecule selection," applicant must further elect a species of cytokine selected from among those recited in claims 178-180, "IL4" OR "IL10" etc.

Method using these different species of culture conditions for the ex vivo education of NKT are independent or distinct because the structures, physicochemical properties and/or mode of action of these species are different, and they do not share a common structure that is

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disclosed to be essential for common utility. In addition, these species are not obvious variants of each other based on the current record.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, or a single grouping of patentably indistinct species, for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

8. There is a search and/or examination burden for the patentably distinct species as set forth above because at least the following reason(s) apply:

The species require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); the prior art applicable to one species would not likely be applicable to another species; and the species are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

9. **Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species to be examined** even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected species**, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The election of the species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the election of species requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected species.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other species.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ZACHARY SKELDING whose telephone number is (571)272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Phuong N. Huynh can be reached on 571-272-0846. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Zachary Skelding/  
Primary Examiner, Art Unit 1644